

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>B-15300 PCT</b>	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, Item 5 below.	
International application No. <b>PCT/IB2005/000506</b>	International filing date (day/month/year) <b>25/02/2005</b>	(Earliest) Priority Date (day/month/year) <b>26/02/2004</b>
Applicant  <b>PHARMA MEDICAL LIMITED</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).

3. ☐ Unity of invention is lacking (see Box III).

**4. With regard to the title,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

**5. With regard to the abstract,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. With regard to the drawings,**

a. the figure of the drawings to be published with the abstract is Figure No. Fig 1/1

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB2005/000506

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C08B37/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C08B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, CHEM ABS Data, PAJ, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CARNEY S L: "EFFECT OF DIACETYL RHEIN ON THE DEVELOPMENT OF EXPERIMENTAL OSTEOARTHRITIS A BIOCHEMICAL INVESTIGATION" December 1996 (1996-12), OSTEOARTHRITIS AND CARTILAGE, BAILLIERE TINDALL, LONDON, GB, PAGE(S) 251-261 , XP001056066 ISSN: 1063-4584 *abstract*	1-36
A	BARBUCCI R ET AL: "Hyaluronic acid hydrogel in the treatment of osteoarthritis" December 2002 (2002-12), BIOMATERIALS, ELSEVIER SCIENCE PUBLISHERS BV., BARKING, GB, PAGE(S) 4503-4513 , XP004377521 ISSN: 0142-9612 *abstract*	1-36

☐ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

29 April 2005

Date of mailing of the international search report

28/06/2005

Name and mailing address of the ISA  
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Authorized officer

Gerber, M

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43*bis*.1)

To:

see form PCT/ISA/220

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/IB2005/000506

International filing date (day/month/year)  
25.02.2005

Priority date (day/month/year)  
26.02.2004

International Patent Classification (IPC) or both national classification and IPC  
C08B37/00

Applicant  
PHARMA MEDICAL LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/IB2005/000506

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/IB2005/000506

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-36
	No: Claims	
Inventive step (IS)	Yes: Claims	1-36
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-21
	No: Claims	22-36

**2. Citations and explanations**

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/IB2005/000506

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1:** CARNEY S L: "EFFECT OF DIACETYL RHEIN ON THE DEVELOPMENT OF EXPERIMENTAL OSTEOARTHRITIS A BIOCHEMICAL INVESTIGATION" December 1996, OSTEOARTHRITIS AND CARTILAGE, BAILLIERE TINDALL, LONDON, GB, PAGE(S) 251-261 , XP001056066 ISSN: 1063-4584
- D2:** BARBUCCI R ET AL: "Hyaluronic acid hydrogel in the treatment of osteoarthritis" December 2002, BIOMATERIALS, ELSEVIER SCIENCE PUBLISHERS BV., BARKING, GB, PAGE(S) 4503-4513 , XP004377521 ISSN: 0142-9612

**1. Novelty**

D1 is concerned with the use of rhein in the treatment of joint disorders and D2 deals with the implementation of hyaluronic acid in the treatment of osteoarthritis.

None of these documents discloses the esterification of hyaluronic acid with rhein.

The subject-matter of claims 1-36 is novel over the cited state of the art (Article 33(2) PCT).

**2. Inventive step**

The hyaluronic acid esterified with rhein exhibits an improved pharmacological activity than hyaluronic acid or rhein alone (see page 17, line 14 - page 18, line 2, as well as figures 4 and 5).

The technical problem underlying the present application is the provision of a compound based on hyaluronic acid with improved pharmacological activity.

None of the cited documents cited alone or in combination would have prompted the

skilled person seeking to solve the above-mentioned technical problem to esterify hyaluronic acid with rhein.

The subject-matter of claims 1-36 is therefore considered inventive (Article 33(3) PCT).

**3. Industrial applicability**

**3.1.** The subject-matter of present claims 1-21 appears to comply with the requirements of industrial applicability as stipulated in Article 33(4) PCT.

**3.2.** Claims 22-36 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).